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| Reference N.92288A AB/HJW | Application No./Patent No. 08020946.3 - 2403 / 2034030 |
| Applicant/Proprietor Sagres Discovery, Inc. | |

Communication

The extended European search report is enclosed.

The extended European search report includes, pursuant to Rule 62 EPC, the European search report (R. 61 EPC) or the partial European search report/ declaration of no search (R. 63 EPC) and the European search opinion.

Copies of documents cited in the European search report are attached.

☒ 2 additional set(s) of copies of such documents is (are) enclosed as well.

The following have been approved:

☒ Abstract

☒ Title

☐ The Abstract was modified and the definitive text is attached to this communication.

The following figure(s) will be published together with the abstract:

Refund of the search fee

If applicable under Article 9 Rules relating to fees, a separate communication from the Receiving Section on the refund of the search fee will be sent later.





EUROPEAN SEARCH REPORT

Application Number
EP 08 02 0946

| DOCUMENTS CONSIDERED TO BE RELEVANT | | | |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------|-----------------------------------------|
| Category | Citation of document with indication, where appropriate, of relevant passages | Relevant to claim | CLASSIFICATION OF THE APPLICATION (IPC) |
| E | WO 03/053224 A (SAGRES DISCOVERY [US]; MORRIS DAVID W [US]; ENGELHARD ERIC K [US] SAGR) 3 July 2003 (2003-07-03) * claims 6-19; table 6 * * page 3, paragraph 6 * * page 26, paragraph 2 * | 1-15 | INV. C12Q1/68 |
| A | MURAMATSU AND R L KINCAID T ET AL: "Molecular cloning and chromosomal mapping of the human gene for the testis-specific catalytic subunit of calmodulin-dependent protein phosphatase (Calcineurin A)" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, ACADEMIC PRESS INC. ORLANDO, FL, US, vol. 188, no. 1, 15 October 1992 (1992-10-15), pages 265-271, XP002124889 ISSN: 0006-291X * the whole document * | | |
| P,A | WO 02/46467 A (IPSOGEN [FR]; BERTUCCI FRANCOIS [FR]; HOULGATTE REMI [FR]; BIRNBAUM DA) 13 June 2002 (2002-06-13) * table 4; sequence 19 * | | TECHNICAL FIELDS SEARCHED (IPC) C12Q |
| The present search report has been drawn up for all claims | | | |
| Place of search Munich | | Date of completion of the search 10 June 2009 | Examiner Persson, Anna |
| CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document | | | |

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 08 02 0946

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.
The members are as contained in the European Patent Office EDP file on
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10-06-2009

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
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| WO 03053224 A | 03-07-2003 | AU 2002364052 A1 | 09-07-2003 |
| | | AU 2008203436 A1 | 21-08-2008 |
| | | CA 2470844 A1 | 03-07-2003 |
| | | EP 1469769 A2 | 27-10-2004 |
| | | JP 2005512558 T | 12-05-2005 |
| WO 0246467 A | 13-06-2002 | AU 3479902 A | 18-06-2002 |
| | | CA 2430981 A1 | 13-06-2002 |
| | | EP 1353947 A2 | 22-10-2003 |
| | | JP 2004537261 T | 16-12-2004 |
| | | JP 2008178411 A | 07-08-2008 |
| | | US 2003143539 A1 | 31-07-2003 |

The examination is being carried out on the **following application documents**:

Description, Pages

1-244 as originally filed

Sequence listings part of the description, Pages

1-6731 as originally filed

Claims, Numbers

1-15 as originally filed

Divisional application - Article 76(1) EPC

1. **Claims 1-14** do not fulfill the requirements of Article 76(1) EPC.
 - 1.1. **Claim 1** discloses a method for diagnosing carcinoma comprising detecting increased expression of PPP3CC, wherein the control comprises normal tissue of the same tissue type.

There is no basis in the earlier application for PP3CC being upregulated in carcinoma, PPP3CC is only mentioned in general as a diagnostic marker in Table 108. Furthermore, although claim 11 of the earlier application provides a basis for a method of diagnosing carcinoma comprising detecting differential expression of PPP3CC, there appears to be no basis for the control comprising normal tissue of the same tissue type, only comparison with a second normal tissue type is disclosed. Furthermore, there appears to be no basis for a method of diagnosis detecting a homologue of PPP3CC.

The last two objections also apply to **claim 2**. The same objections as for claim 1 also apply to dependent **claim 13**.

1.2. **Claim 3** discloses a method of diagnosing e.g. prostate cancer comprising contacting SEQ ID NO:1587 from a prostate sample and a control sample with a probe and comparing the amount of duplex formed. No basis can be found for this subject-matter in the earlier application.

1.3. **Claim 4** discloses a method of screening drug candidates comprising contacting a cell expressing a gene comprising SEQ ID NO:1587 or a homologue thereof with a drug candidate and detecting a two fold reduction in the expression level of PPP3CC.

No basis can be found in the earlier application for said limit of two fold difference in expression level in relation to drug screening. Furthermore there is no basis for PPP3CC expression being reduced by anti-cancer drugs. Furthermore there appears to be no basis for said method using a gene comprising a homologue of SEQ ID NO:1587. Furthermore there is only a basis for *diagnosing* stomach cancer (in [0024]) but not for screening for a drug treating said cancer.

The objection to "gene comprising a homologue" also applies to **claims 5-10 and 14**.

1.4. **Claim 9** discloses the medical use of an inhibitor of a CA protein for treating e.g. stomach cancer, wherein the CA protein is encoded by a gene comprising a homologue of SEQ ID NO:1587. There is only a basis in the earlier application for *diagnosing* stomach cancer (in [0024]) but not for treating said cancer.

1.5. **Claim 11** discloses a method for diagnosing carcinoma comprising sequencing a CA gene comprising or encoding a nucleotide sequence at least 98% identical to SEQ ID NO:1587. There appears to be no basis in the earlier application for a CA gene *comprising* SEQ ID NO:1587 or a homologue thereof.

1.6. **Claim 12** discloses a method of determining gene copy number using a probe comprising SEQ ID NO:1587 or a homologue thereof. Although there is a basis in the earlier application for a CA gene used as a probe (in [0212]), there appears to

be no basis for a probe *comprising* SEQ ID NO:1587 or a homologue thereof.

2. The claim features without a basis in the earlier application are not considered when assessing novelty of the present application.

Novelty - Article 54 EPC

3. The present application does not meet the requirements of Article 52(1) EPC because the subject-matter of **claims 1-15** is not new within the meaning of Article 54(1) and (3) EPC.

PCT application No. WO03/053224 published on 03-07-2003 claims the valid priority date of 20-12-2001. It has been supplied to the European Patent Office in one of its official languages according to Article 153(3) and (4) EPC and the filing fee provided for in Rule 159(1)(c) EPC or Article 39(1) PCT has been paid. The requirements of Rule 165 EPC are thus fulfilled.

Its content as filed is therefore considered to be comprised in the state of the art relevant to the question of novelty, pursuant to Article 54(3) EPC. This earlier application shows:

- A method for diagnosing carcinoma comprising determining differential expression of SEQ ID NO:1587 (PPP3CC) (claim 11, Table 6), wherein e.g. stomach cancer can be diagnosed (p3 par. 6) and wherein the change in expression is e.g. 100% (p26 par. 2).
- A method of screening drug candidates comprising comparing the expression of SEQ ID NO:1587 in the presence and absence of the drug candidate (claims 6-7).
- A method for screening for a bioactive agent capable of binding to or modulating the activity of a protein encoded by SEQ ID NO:1587 (claims 8-9).
- A method of evaluating the effect of a candidate carcinoma drug comprising determining alterations in expression or activation of PPP3CC (claim 10).
- A method for inhibiting the activity of a protein encoded by SEQ ID NO:1587 (claim 12) as well as a related medical use (claim 13).
- A method of neutralising the effect of a protein encoded by SEQ ID NO:1587 (claim 14).

- A method of diagnosing carcinoma by sequencing PPP3CC (claim 18).
- A method of determining CA gene copy number using a PPP3CC probe (claim 19).
- An antibody specifically binding a protein encoded by SEQ ID NO:1587 (claim 16).
- A biochip comprising a nucleic acid segment of SEQ ID NO:1587 (claim 17).

Thus, it is prejudicial to the novelty of the subject-matter of **claims 1-15** of the present application.

Exceptions to patentability - Article 53 EPC

4. **Claims 8 and 10** disclose methods for respectively inhibiting the activity and neutralising the effect of a PPP3CC protein. These are interpreted as methods of treatment, which are excluded from patentability according to Article 53(c) EPC.

Sufficiency of disclosure. Clarity and Support- Articles 83 and 84 EPC

5. The application does not meet the requirements of Articles 83 and 84 EPC, because **claims 1-11 and 13-15** are not clear, fully supported and/or sufficiently disclosed.
 - 5.1. **Claim 2** discloses a method for diagnosing carcinoma comprising detecting differential expression of SEQ ID NO:1587 (PPP3CC), but without specifying whether the expression is up- or downregulated in carcinoma. It is consequently unclear and insufficiently disclosed how to perform the method of diagnosis of claim 2.

The same applies to dependent **claim 13**. The same also applies to **claim 11**, wherein it is not disclosed how to use the sequencing result to diagnose carcinoma.

- 5.2. It is unclear what is meant with "a gene... *encoding* a nucleotide sequence" in

claim 4. The same applies to **claims 5-11 and 14.**

- 5.3. **Claim 15** discloses a biochip comprising segments of SEQ ID NO:1587 or fragments thereof. It is unclear how short these fragments can be. It is furthermore unclear what is the difference between segments and fragments.
- 5.4. There is no support in the application as filed that SEQ ID NO:1587 is upregulated in carcinoma, nor that its downregulation/inhibition would be useful for treating carcinoma. This applies to **claims 1, 3-4 and 9.**

Conciseness - Article 84 EPC

6. **Claims 1-4, 7-8 and 10-11** have been drafted as separate independent claims.

Under Article 84 in combination with Rule 43(2) EPC, an application may contain more than one independent claim in a particular category only if the subject-matter claimed falls within one or more of the exceptional situations set out in paragraph (a), (b) or (c) of Rule 43(2) EPC. This is not the case in the present application, however, for the following reasons:

- Claims 1-3 and 11** all disclose methods of diagnosing prostate, colon, stomach or breast cancer.
- Claims 4 and 7** both relate to methods evaluating the ability of drug candidates to alterate the expression level of SEQ ID NO:1587.
- Claims 8 and 10** both relate to methods for inhibiting/neutralising the activity/effect of a protein encoded by SEQ ID NO:1587.

In the further prosecution of the application, failure to file an amended set of claims which complies with Rule 43(2) EPC may lead to refusal of the application under Article 97(2) EPC.

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